Summary of Imazalil

Uses

- Registered for post-harvest treatment of citrus fruits, for seed treatment of barley and wheat prior to planting, and in egg handling facilities. There is also an import tolerance for bananas. Previously submitted petitions to add certain new uses and to establish new tolerances for pears, melons, and sweet corn will be assessed during the development of the RED.

Health Effects

- Placed in Category II, III and IV for oral, dermal, and inhalation toxicity, respectively. Imazalil is highly irritating to eyes (Category I), but is not a skin irritant (Category IV) or a dermal sensitizer.

- The primary target organ for imazalil toxicity in animals is the liver.

- Carginogenicity studies in rodents find that imazalil is carcinogenic to male mice and rats, based on significant increases in liver adenomas and combined adenomas/carcinomas. Imazalil has been classified as "likely to be carcinogenic in humans."

FQPA Safety Factor

- The FQPA Safety Factor is 3X for both the acute and chronic assessments due to the absence of acute, subchronic, and developmental neurotoxicity studies. The use of an additional 3X factor for the chronic assessment was warranted due to susceptibility of neonates observed in the two-generation reproduction study in rats. As a consequence, the safety factor was retained at 10X for the assessment of chronic dietary risk and reduced from 10X to 3X for the assessment of acute dietary risk for females 13 – 50 years old.

Health Risk

- Acute risk estimates from exposure to residues in food do not exceed the Agency's level of concern. The estimated acute dietary risk (food only) is 15% of the aPAD at the 99.9^{th} percentile for the sub-population, females (13-50 years), the only subpopulation at risk.

- Chronic risk estimates from exposure to residues in food do not exceed the Agency's level of concern. The chronic dietary (food only) risk estimate is <3% of the cPAD, for the U.S. Population and all sub-populations.

- Regarding cancer, the Agency has not yet made a final determination for imazalil concerning whether the linear low-dose (Q_1*) model or a threshold cancer model is most appropriate. The registrant is currently conducting studies to address this issue. In the interim, the Agency has utilized the more conservative standard Q_1* model in the current risk assessment. The cancer dietary risk estimate for imazalil using the Q_1* model is 2.1×10^{-6} $(mg/kg/day)^{-1}$, which is within the range of cancer risks for which Agency does not have a concern.

Drinking Water Assessment

- The Agency believes that no population group is exposed to imazalil residues in drinking water at a level that poses an acute or chronic risk of concern because the registered uses are unlikely to contaminate surface or ground waters.

- Although cancer DWLOCs were not calculated since the cancer "risk cup" was full, the Agency has qualitatively concluded that humans will not be exposed to imazalil in drinking water at levels that will appreciably affect the cancer risk.

Aggregate Risk

- There are no residential uses of imazalil; therefore, aggregate risk includes only the food and drinking water risks described above.

Tolerance Reassessment Summary

- Higher tolerances are required for barley and wheat grains to reflect the sensitivity of the data-collection method and to account for apparent residues in/on control grain samples

- Data from citrus processing studies showed that imazalil residues do not concentrate in juice, but do concentrate in oil; therefore the reassessed tolerance for citrus oil is 200 ppm.

- Established tolerance for banana pulp is revoked due to Agency policy to establish a tolerance on the whole commodity

- Tolerance for cottonseed revoked because there are no registered uses of imazalil on cottonseed

- Tolerances for animal muscle, fat, meat by-products, liver, and milk are increased based on feeding studies.

Data Requirements

Toxicology Data for OPPTS Guidelines:

- 870.6300 Developmental Neurotoxicity in Rats
- 870.6200 Acute Neurotoxicity Study in Rats
- 870.6200 Subchronic Neurotoxicity Study in rats

Product and Residue Chemistry Data for OPPTS Guidelines:

- 860.1340 Residue analytical Method - Animal Commodities
- 860.1360 Multiresidue Method
- 860.1480 Egg and poultry fumigation Study

Occupational Exposure Data for OPPTS Guidelines

- Exposure study of citrus treatment applicators (wax application and foamers)
- Post application inhalation and dermal exposure following smoke generator or spraying applications in chicken hatcheries